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Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : STEINMAN, ET AL.

Serial No. : 08/261,537

Group Art Unit: 1808

Filed : June 17, 1994

Examiner: B. Lankford

For : METHOD OF IN VITRO PROLIFERATION OF
DENDRITIC CELL PRECURSORS AND THEIR
USE TO PRODUCE IMMUNOGENS

Assistant Commissioner of Patents
and Trademarks
Washington, D.C. 20231

DECLARATION UNDER 37 CFR § 1.131

I, Ralph M. Steinman, declare that:

1. I am presently Professor and Senior Physician of the Laboratory of Cellular Physiology and Immunology at Rockefeller University, 1230 York Avenue, New York, New York 10021-6319.

2. I am one of the inventors of the above-identified patent application, along with Gerold Schuler and Kayo Inaba.

3. I have read and understand the Office Action dated October 19, 1996 in which the Examiner cited Sallusto and Lanzavecchia, Journal of Experimental Medicine,

179:1109-1118, April 1994 in support of a rejection under 35 U.S.C. § 103 as teaching the use of granulocyte macrophage colony structuring factor (GM-CSF) and interleukin 4 (IL-4) to culture dendritic cells.

4. The instant application discloses and claims the culturing of proliferating dendritic cells in the presence of GM-CSF and an inhibitor of maturation of non dendritic cell precursors, such as IL-4. Culturing of dendritic cell precursors in the presence of GM-CSF typically results in proliferating dendritic cells clustered in an adherent "cell ball" (see the instant specification: Examples 1-8, pages 50 to 101). The addition of an inhibitor of maturation of non dendritic cell precursors facilitates the growth of the proliferating dendritic cell balls.

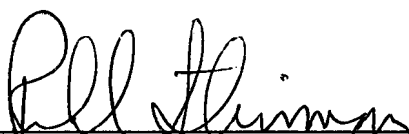
5. As a co-inventor in the above identified application, I communicated with Drs. Schuler and Inaba regarding several aspects of the instantly claimed invention. Such a communication is illustrated in the attached facsimile letter (attached as Exhibit 1) from Dr. Schuler to myself.

6. The photocopy of the facsimile letter (attached as Exhibit 1) sent to me by Dr. Schuler, was received by me in the United States prior to March 24, 1994. This describes the addition of IL-4 to proliferating cultures of dendritic cells in GM-CSF. Page 2, lines 10-16. The letter details how the addition of IL-4 inhibits the formation of non-dendritic cells (the so called "bad balls") but surprisingly does not inhibit the formation of

proliferating dendritic cell balls. Therefore, our invention as disclosed and claimed in the present application was complete in the U.S. prior to the publication of Sallusto and Lanzavecchia. Moreover, my receipt of this facsimile letter, which describes the culturing of dendritic cells in the presence of GM-CSF and IL-4, confirms my involvement in the United States in the making of this invention.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: Aug 2, 1996



RALPH M. STEINMAN, M.D.